REMARKS

Rejection of Claims and Traversal Thereof

In the March 6, 2009 Office Action:

claims 66, 69 and 71 were rejected under 35 U.S.C. §112, second paragraph;

claims 60-61, 63-65, 67-70 and 72 were rejected under 35 U.S.C. §103(a) as being unpatentable over JP 06-070698 (hereinafter Sugimoto) in view of Borror et al. (U.S. Patent No. 6,036,992) in view of Gladue et al. (WO 99/06585);

claim 62 was rejected under 35 U.S.C. §103(a) as being unpatentable over Sugimoto in view of Borror et al. in view of Gladue et al. as applied above in view of Place et al. (US Patent No. 6,261,590):

claim 66 was rejected under 35 U.S.C. §103(a) as being unpatentable over JP 06-070698 (hereinafter Sugimoto) in view of Gladue et al. (WO 99/06585) and in further view of Shao (Aquaculture Pharmaceuticals and biological: Current Perspectives and Future Possibilities): and

claim 71 was rejected under 35 U.S.C. §103(a) as being unpatentable over JP 06-070698 (hereinafter Sugimoto) in view of Borror et al. (U.S. Patent No. 6,036,992) in view of Gladue et al. (WO 99/06585) and in view of Robies Median et al. (Downstream Processing of Algal Polyunsaturated Fatty Acids).

These rejections are hereby traversed and reconsideration of the patentability of the pending claims is therefore requested in light of the following remarks.

Rejection under 35 U.S.C. §112, second paragraph

Claims 66, 69 and 71 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants have amended the claims thereby obviating this rejection and request withdrawal of same.

Rejections under 35 U.S.C. §103(a)

In the October 29, 2009 Office Action, claims 60-61, 63-65, 67-70 and 72 were rejected under 35 U.S.C. §103(a) as being unpatentable over Sugimoto, in view of Borror and in view of Gladue. Applicants traverse such a rejection.

Applicants' claimed invention is recited in method claim 60:

> 60. A method of preparing a coldwater fish feed composition which provides for an increased level of carotenoids in the fish consuming same, the method comprising (a) mixing a carotenoid and phospholipids to form a mixture, wherein the phospholipids have at least 20% fatty acid residues with 4 or more double bonds and are found in PUFA-rich extracts of single cell microorganisms and are liquid at the body temperature of the-coldwater fish; and (b) thereafter combining the mixture with at least one other animal feed component, such that the carotenoid makes up at least 1%, by weight, of the composition and the phospholipid makes up at least 5%, by weight, of the composition.

It should be noted that applicants' invention is a method of producing a feed for coldwater fish that provides for the availability and stability of carotenoids by combining such carotenoids with phospholipids, wherein the phospholipids have at least 20% fatty acid residues with 4 or more double bonds and are found in PUFA-rich extracts of single cell microorganisms. Importantly the fatty acid residues with 4 or more double bonds are liquid for consumption by a coldwater fish and increasing the efficacy of the carotenoid absorption at low temperatures. Equally important, the carotenoid makes up at least 1%, by weight, of the feed composition and the phospholipid makes up at least 5%, by weight, of the feed composition. None of the prior art reference, either alone or in combination, teaches or suggests the presently claimed invention.

According to the Office,

While Sugimoto does not expressly state the range of a carotenoid to be at least 1%, it is encompassed by the range taught by Sugimoto. Sugimoto teaches that the composition comprises at least 2g phospholipid (at least 2% of the feed) and at least 3mg carotenoid (at least 0 003% of carotenoid) per 100g of feed. Sugimoto also claims the carotenoid to be at least 3 mg per 100g of feed and the phospholipid to be at least 2g per 100g of feed. It would have been obvious to one of skill in the art to adjust and optimize the amount of carotenoid dependent on the animal to be fed or the components of the feed and particularly, to increase and optimized the amount of carotenoid to improve the color in the animal meat (e.g. salmon) as it is visually more appealing to consumers. The amount of phospholipid would increases proportionally as the additive requires blending 100g of phospholipid with 0.1-10g of carotenoid.

Applicants question why the Office is completely overlooking paragraph 12 of the Sugimoto reference wherein the Sugimoto reference clearly describes a range for the use of the phospholipid and carotenoid components, as recreated below:

> "[0012]Although it is 0.1g/100g feed -10g/100g feed, quantity added in feed is added so that it may become the amounts 2g-10g of phospholipid/100g feed, and the amount of carotenoid **of 3 mg - 100 mg/100g feed preferably."** (emphasis added)

Thus, Sugimoto reference does include an upper limit, that being from 0.003% to 0.1% for the carotenoid in 100 g of feed as shown below by the simple conversion from weight units to percent units, wherein "C" represents carotenoid:

$$3 \text{ mg of C} = \frac{1 \text{ g of C}}{1000 \text{ mg of C}} = 0.003 \text{ g of C.}$$

$$\frac{0.003 \text{ g of C}}{100 \text{ g of Feed}} \times 100\% == 0.003\ \%$$

And

$$100 \text{ mg of C} = \frac{1 \text{ g of C}}{1000 \text{ mg of C}} = 0.1 \text{ g of C.}$$

$$\frac{0.1 \text{ g of C}}{100 \text{ g of Feed}} \times 100\% = 0.1\%$$

Notably, applicants include at least 1% of a carotenoid in the feed composition which is a 100 times more than that taught by Sugimoto. The Sugimoto reference does not in any way describe, teach or suggest this higher level of the carotenoid.

Notably, as previously stated numerous times, the Sugimoto group found low percentages of carotenoids in the feed composition to be very effective, and as such, why would one skilled in the art be motivated to change the amount of carotenoids in the feed compositions. Notably the examples of Sugimoto showed that 10 mg of carotenoids in 100 g of feed **(.01% by weight of feed)** was effective to reduce the level of formed peroxide (see Table 1, composition (3)).

[0016]Experimental plot :. (1) 3% of a soybean lecithin. (2) Astaxanthin 10mg/100g feed. (3) Process and carry out a vacuum packing to all the fish picking raisings and a fillet at the time of the administration division test termination of a frozen sardine which carried out 10 mg of 3% of 3% of soybean lecithin + astaxanthin 10mg/100g feed (4) soybean lecithin + beta-carotene/100g feed (5) additive-free control plot (6) cutting, -The color of a dark-flesh muscle,

Thus, with the 10mg/100 feed or 0.01% of carotenoid (Sample 3) there was a marked reduction in peroxide concentration of the lipids in the muscles as shown below in Table 1. Notably, lowering the peroxide level reduces smell and blackening of the fish tissue.

[Table 1]

表 1　ブリ筋肉の官能評価と筋肉脂質の過酸化物濃度

試験区	血合筋の鮮やかさ	味	臭い	過酸化物濃度 nmol ／mg脂質
1	41	42	40	0.31（±0.12）
2	35	36	40	0.66（±0.34）
3	48	48	47	0.18（±0.10）
4	47	46	48	0.21（±0.13）
5	31	35	33	1.10（±0.75）
6	12	22	11	1.82（±0.51）

In example 3, Table 3, again the only amount of carotenoid used was 10 mg per 100 grams of feed (.01% of the feed composition).

[0023]experimental plot: -- (1) soybean-lecithin 3%(2) soybean-lecithin 3%+ astaxanthin 10mg/100g feed (3) soybean-lecithin 3%+ opossum shrimp 20%(4) additive-free control plot

[Table 3]
表３　マダイ筋肉毛細血管のメラニン色素沈着の有無（ｃｍ）

試験区	採材部位	Ｓ－１	Ｓ－２	Ｓ－３	合　計
(1) 大豆レシチン	３％	１２	１０	１６	３８
(2) 大豆レシチン	３％	３	６	０	９
アスタキサンチン	10mg				
(3) 大豆レシチン	３％	８	５	５	１８
イサザアミ	20%				
(4) 無添加対照区		７８	６４	５４	１９６

Clearly, sample 2 with (10mg/100g or feed) 0.01% of carotenoid was effective in reducing the negative color effect of the tissue. Thus, as stated above, this reference provides no indication or motivation to change the amount of carotenoids in a feed composition.

According to the Office:

. It would have been obvious to one of skill in the art to adjust and optimize the amount of carotenoid dependent on the animal to be fed or the components of the feed and particularly, to increase and optimized the amount of carotenoid to improve the color in the animal meat (e.g. salmon) as it is visually more appealing to consumers.

Notably, the Appeal Board in *Ex parte Whalen*, 80 USPQ2d 1078, BPAI 7/2008, recently ruled that if the cited reference teaches a lower value for a specific property, then the cited reference does not lead a person

of ordinary skilled in the art to modify the compositions and increase the level of specific components. As stated by the Board, when the reference teaches that the low level of a component is a desired property, then there is no teaching or suggestion to increase amount of such a component in the composition. As such, the effectiveness of the 0.003 % to 0.1% level of carotenoid in Sugimoto provides the teaching that the low level is desirable.

The Office states that Borror "teaches that the microbial single cell oils may be used, particularly for the ARA and DHA fatty acid components of phospholipids." However, the Office has missed that the Borror reference clearly states that the level of long chain fatty acids ω-6 is **from 0.2 %to about 0.6 %** and more preferably about **0.4 %** of the total lipid blend; and the level of long chain fatty acids ω-3 is from about **0.06 % to about 0.3 %** and more preferably about **0.12 %** of the total lipid blend. Clearly, these levels are very low and the direction of this reference is to stay at the 0.4 percent for ω-6 fatty acids and 0.12 percent ω-3 fatty acids (see column 4, lines 33-36 of Borror). Thus, where is there any guidance to go in the direction of applicants' claimed invention? There is none, and thus this proposed combination does not teach or suggest the presently claimed invention.

Again, the *Ex parte Whalen* decision is relevant because if the cited reference teaches a lower value for a specific property, then the cited reference does not lead a person of ordinary skilled in the art to modify the compositions and increase the level of specific components. When Borror describes the amount of long chain fatty acids, the amounts are narrowed to the center of the range and kept at the low amount of 0.4 percent for ω-6 fatty acids and 0.12 percent ω-3 fatty acids. Thus, Borror does not provide any suggestion to "optimized" the level of the DHA fatty acid components of phospholipids, and raise the levels to at least 5 % of the feed or 20% of the lipids.

With regards to Gladue, the Office recited that Gladue teaches that aquaculture feed needs to be nutritionally balanced so that the fish larvae receive proper nutrition and DHA significantly contributes to larval growth and survival. The Office contends that because Gladue discusses the use of DHA in feed that there is some teaching in Gladue that such DHA (PUFA) increases the stability and absorption of the carotenoid. IT DOES NOT.

Applicants' claimed invention relates to a method of preparing a coldwater fish food composition that upon administration increases the take-up of carotenoids into the fish tissue. One skilled in the art considering Sugimoto and Gladue would not know that carotenoids such as astaxanthin are difficult to

incorporate in coldwater fish and that combining the carotenoids with phospholipids found in PUFA-rich extracts of single cell microorganisms would significantly increase the uptake of the carotenoids in the muscle tissue of said coldwater fish.

Applicant insists that the Office's statement that "optimizing is obvious" is very similar to an "obvious to try" rejection. It is also important for the Office to review the "*In re Kubin*" ruling decided on April 3, 2009 (See I*n re Kubin*, 90 USPQ2d 1417 (Fed. Cir. 2009)).

Specifically, the *Kubin* Court revisited the *In re O'Farrell* decision (*In re O'Farrell*, 853 F.2d 894(Fed Cir. 1988)) and discussed that to differentiate between proper and improper applications of "obvious to try," the O'*Farrell* Court outlined two classes of situations where "obvious to try" is erroneously equated with obviousness under §103. In the first class of cases:

> what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

In such circumstances, wherein metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness.

The second class of *O'Farrell's* impermissible "obvious to try" situations occurs where

> what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

KSR affirmed the logical inverse of this statement by stating that §103 bars patentability unless "the improvement is more than the predictable use of prior art elements according to their established functions." Clearly, applicant has shown improvement far surpassing any predictable use of any combination of PUFA fatty acids and carotenoids.

Importantly, applicants have provided unexpected and superior results by using the feed of the present invention that includes phospholipids found in PUFA-rich extracts of single cell microorganisms in combination with carotenoids. For example, applicants used the components of Sugimoto as a comparison and to show the effectiveness of the PUFA-rich extracts of single cell microorganisms. When

applicants incorporated a mixture of soy lecithin and *Phaffia* yeast (a natural source of astaxanthin) into the feed for trout (a coldwater fish), there was an increase in the uptake of the carotenoid in the muscle tissue (see Figure 1 reproduced hereinbelow wherein the increase was about 34% higher than without the soy lecithin). However, unexpectedly, when applicants incorporated a mixture of phospholipids found in PUFA-rich extracts of single cell microorganisms with high content of DHA and *Phaffia* yeast in the feed for trout, there was a 56% higher assimilation of the carotenoid in the muscle tissue of the fish than without the PUFA.

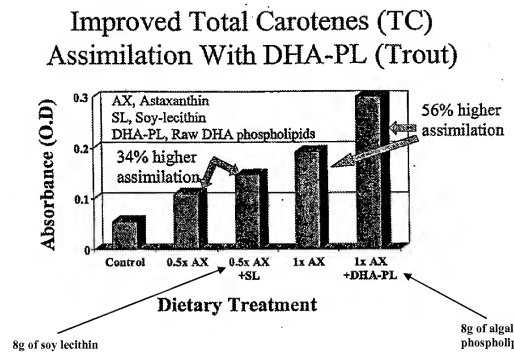

Figure 1 set forth above shows the improved total carotenoid content of rainbow trout using conditions as described in Example 5 (for the Astaxanthin compared to Astaxanthin+DHA-phospholipid and using **8g of the algal DHA-phospholipid**) and Example 4 (for Astaxanthin compared to Astaxanthin +soy lecithin and **using 8g of the soy lecithin**). The control had no added astaxanthin in the diet (some residual carotenoids were in the original diet). The soy lecithin gave a 34% higher incorporation of astaxanthin (AX) than AX alone. However, the DHA-rich phospholipid gave 56% higher incorporation of AX than AX alone and **almost 100% greater absorption than using the soy lecithin. It is important to note that both the compositions of Example 4 and 5 contain exactly the same amount of a phospholipid but the one that is derived from microorganisms and included DHA-rich**

phospholipids is surprisingly more effective in aiding the absorption of the carotenoid. Clearly, almost a 100% increase in the incorporation of the carotenoid into the fish by using the algal derived DHA-phospholipids by applicants is totally unexpected.

It is important to note that the compositions used in the dietary treatments in the figure above contain exactly the same amount of a phospholipid but the one found in PUFA-rich extracts of single cell microorganisms is surprisingly more effective in aiding the absorption of the carotenoid. One skilled in the art considering Sugimoto, Borror and Gladue would not reasonably expect that the use of phospholipids found in PUFA-rich extracts of single cell microorganisms with the carotenoids would significantly increase the uptake of carotenoids in the muscle tissue of coldwater fish.

According to the Office, the results shown by applicants in the present invention are not unexpected and the 40% increase is not sufficient. The Office cites Bustos, et al. (2003, *J. of Food Eng.* 56, 289-293) as evidence for a lack of unexpected results because the Office believes that Bustos teaches the stability of long chain PUFAs and astaxanthin.

Applicants reviewed the Bustos, et al. reference and specifically section 3.2 cited by the Office and found that the stability of the krill oil is due to the high levels of tocopherols along with carotenoid pigments could be responsible, as shown below:

Fig. 2A shows that chitosan microencapsulation did not have a major effect on the oxidative stability of the krill oil. It is remarkable, however, that even in the unprotected oil, the polyene ratio did not decrease significantly during the first 15 days of the study. This result indicates that krill oil would have an intrinsic factor of stability which avoids oxidation of EPA, DHA (Kolakowska, 1988). This phenomenon has also been observed by Japanese researchers who have suggested that the high content of tocopherols along with carotenoid pigments could be responsible for such high oxidative stability of Antarctic krill oil since both substances are well recognized natural anti oxidants (Suzuki & Shibata, 1990). To certain extent, these ob-

Tocopherols include a group of closely related, fat-soluble alcohols that behave similarly to vitamin E and are present in milk, lettuce, and wheat germ oil and certain other vegetable oils. Thus the stability was not found to be due to the PUFA but instead the fat soluble alcohols. Further, when the carotenoid pigments were removed from the presence of the tocopherols, the only thing that saved them from

oxidation was the chitosan microencapsulation. Thus, from the Bustos reference the only indication of stability is from the tocopherols and chitosan encapsulation and the Office needs to reconsider the unexpected results shown by applicants because one skilled in the art considering Sugimoto, Borror and Gladue would not know that carotenoids such as astaxanthin are difficult to incorporate in coldwater fish and that combining the carotenoids with phospholipids found in PUFA-rich extracts of single cells algal organisms would significantly increase the uptake of the carotenoids in the muscle tissue of said coldwater fish.

For the reasons discussed hereinabove, the Office has not met its burden of establishing a *prima facie* case of obviousness. Applicants therefore request that the rejection of claims 60-61, 63-65, 67-70 and 72 on the basis of obviousness be withdrawn.

2. In the September 29, 2009 Office Action, claim 62 was rejected under 35 U.S.C. §103(a) as being unpatentable over Sugimoto in view of Borror and Gladue as applied above in view of Place et al. (US Patent No. 6,261,590) (hereinafter Place). Again, applicants insist that the combination of Sugimoto, Borror, Gladue and Place does not defeat the patentability of the presently claimed invention. The shortcomings of Sugimoto, Borror and Gladue, as discussed above, are not overcome by the introduction of Place. This is also applicable to the rejections for claims 66 and 71 because the added and new references do not overcome the shortcomings of the combination of Sugimoto, Borror and Gladue. Applicants submit that the Office has not established a *prima facie* case of obviousness and requests that all rejections under section 103 be withdrawn.

Fees Payable

No fee is due for entry of this amendment; however, if a fee is found due for entry of this amendment, the Commissioner is authorized to charge such fee to Deposit Account No. 13-4365 of Moore & Van Allen.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Huang reconsider the patentability of the pending claims in light of the distinguishing remarks herein, and withdraw all rejections, thereby placing the application in condition for allowance. If any issues remain

outstanding incident to the allowance of the application, Examiner Huang is requested to contact the undersigned attorney at (919) 286-8090.

Respectfully submitted,

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